

**REMARKS**

Claims 2, 5-9, 11-19, 24 and 25 are pending in the application; claims 2, 5, 6, 11, 12, 15, 16, 24 and 25 have been rejected; claims 7-9, 13, 14 and 17-19 have been withdrawn from consideration.

Amendment of claims 24 and 25 to limit the strains of virus to proliferative and non-proliferative adenovirus may be found in claim 2, and in the specification, such as in paragraphs [0011] and [0013]. Applicants also note that this is the elected species.

Amendment of claim 11 to recite the induction of a cytotoxic T lymphocyte (CTL) reaction in the subject may be found throughout the specification, such as in paragraphs [0009], [0010], [0017], etc.

Further amendments to the claims are being made to place them more fully in proper U.S. claim format and to make the claims more clear.

Upon entry of the amendment claims 1-4, 10 and 20-23 will be canceled and claims 5-9, 11-19, 24 and 25 will be pending.

No new matter has been added. Entry of the amendment is respectfully requested.

**I. Election**

At page 2 of the Office Action, the Examiner summarizes the status of the species election. Applicants understand that upon allowance of the elected species, the Examiner will expand his search to the non-elected species encompassed by the generic claims.

**II. Priority**

At pages 2-3 of the Office Action, the Examiner notes that the present application is a 371 of PCT/JP04/15220, filed October 15, 2003. Applicants note that the correct filing date of the international application is October 15, 2004. The correct date is provided on the application data sheet filed with the applications. Applicants are submitting herewith a requested for a corrected official filing receipt to correct the error in the U.S. PTO database.

The Examiner goes on to state that because a certified translation into English of international application PCT/JP04/15220 has not been filed, the effective filing date of the instant application is the date of national stage entry, namely April 14, 2006.

In response, Applicants respectfully note that a *certified* translation into English of an international application is not required in order to have the U.S. PTO recognize the filing date of the international application (see, e.g., MPEP §1893.01(d)). Indeed, as noted in the Notice of Acceptance of Application Under 35 U.S.C. 371, mailed March 12, 2007 by the U.S. PTO, all requirements for national stage entry under 35 U.S.C. 371 have been met by Applicants. Therefore, all requirements under 35 U.S.C. §371 have been met and the filing date of the instant application is the filing date of the international application, namely, October 15, 2004.

Finally, Applicants are submitting herewith a certified translation into English of the priority application JP 2003-354983, filed October 15, 2003, thereby perfecting Applicants' claim to priority of the prior Japanese application. Applicants respectfully request acknowledgement of the same by the Examiner in the next office communication.

### **III. Specification**

At page 3 of the Office Action, the Examiner objects to the specification, stating that the description of Figures 25(a) and 25(b) in the body of the specification differs from that of the figure legend for Figure 25.

In response, Applicants respectfully note that the description providing in paragraphs [0124] and [0125] of the specification, and the figure legends of Figures 25(a) and (b), are correct as written. In particular, as discussed in paragraph [0124] adenovirus (Ad- $\beta$ -gal) was administered to three different groups of mice. A first group received one dose of virus, a second group received two doses of the virus, and the third group received three doses of the virus.

Next, as described in paragraph [0125], some of the mice from each of these three groups received both A549 cells and 293 cells. The results of the combined effects of the

Ad- $\beta$ -gal virus and the two types of carrier cells are shown in Figure 25. Figure 25(a) shows the changes in tumor volumes in mice from the first group (“x1 injection of Ad- $\beta$ -gal”), second group (“x2 injection of Ad- $\beta$ -gal”) and third group (“x3 injection of Ad- $\beta$ -gal”), where the mice of each of these three groups received both A549 cells and 293 cells. Figure 25(b) shows the survival rates for the same groups of mice (receiving one, two or three injections of adenovirus, and receiving both A549 cells and 293 cells).

As further explained in paragraph [0125], some of the mice from each of the three noted groups received only A549 cells. The results of the combined effects of the Ad- $\beta$ -gal virus and the A549 cells are shown in Figure 26. Figure 26(a) shows the changes in tumor volumes in mice from the first group (“x1 injection of Ad- $\beta$ -gal”), second group (“x2 injection of Ad- $\beta$ -gal”) and third group (“x3 injection of Ad- $\beta$ -gal”), where the mice of each of the three groups received only A549 cells. Figure 26(b) shows the survival rates for the same groups of mice (receiving one, two or three injections of adenovirus, and receiving only A549 cells).

In view of these comments, reconsideration and withdrawal of the rejection is respectfully requested.

#### **IV. Claim Rejections Under 35 U.S.C. 112**

**A.** At pages 3-4 of the Office Action, claim 25 is rejected as being indefinite under 35 U.S.C. 112, second paragraph.

The Examiner states that the reference in claim 25 to a carrier cell is indefinite.

Included herewith is an amendment to claim 25 such that the claim now more clearly recites the carrier cells. The claim is now definite as amended. Applicants therefore respectfully request reconsideration and withdrawal of this rejection.

**B.** At page 4 of the Office Action, claims 2, 5-6, 11-12, 15-16 and 24-25 are rejected as failing to comply with the written description requirements under 35 U.S.C. 112, first paragraph.

The Examiner states that claims 24-25 recite the administration of a population of carrier cells before the virus and that such a recitation is not adequately described in the specification as written.

Included herewith is an amendment to claims 24 and 25 such that the claims now more clearly recite the carrier cells and the means by which they are utilized. In particular, the claims recite the use of a population of carrier cells in only one instance (administration after the non-proliferative adenovirus is given to a subject). The specification fully supports the claims as amended. Applicants therefore respectfully request reconsideration and withdrawal of this rejection.

**V. Claim Rejections Under 35 U.S.C. 103(a)**

**A.** At page 7 of the Office Action, claims 2, 11-12 and 24-25 are rejected as being unpatentable under 35 U.S.C. 103(a) in view of Szalay (US 2005/0031643, dated June 18, 2004), Molnar-Kimber (1999) and Harrison (2001).

The Examiner states that Szalay discloses the method of claim 25, with Molnar-Kimber teaching the missing element of administering the oncolytic virus infected carrier cell to the patient to make the oncolytic virus act on a tumor cell within the patient, and Harrison teaching the missing element of the A549 carrier cell. The Examiner concludes that it would have been obvious to the skilled artisan to combine the teachings of the noted publications to arrive at the present invention as claimed.

In response, Applicants respectfully note that Szalay is not legally-effective prior art against the pending claims. In particular, and as discussed above, Applicants have perfected their claim to priority to JP 2003-354983, filed October 15, 2003. Further, the invention as now claimed is fully supported in the translated priority document, such as in paragraphs [0010], [0013], [0015], [0018], [0044]-[0053] and [0065]-[0069], and in Example 3 and Claim 4. Thus, the priority date of the instant application is October 15, 2003.

In contrast to the Examiner's suggestion to the contrary, the Szalay publication (US 2005/0031643) is only entitled to the application filing date (June 18, 2004) under 35 U.S.C. §102(e). As Szalay is not a published application filed in the U.S. prior to the date of invention of the instant application, Szalay may not serve as legally-effective prior art against the instant application.

Moreover, neither Molnar-Kimber nor Harrison, alone or in combination, teaches each element of claim 24 or 25.

The Examiner has therefore not established a *prima facie* showing of obviousness under 35 U.S.C. §103(a) and Applicants respectfully request reconsideration and withdrawal of this rejection.

**B.** At page 12 of the Office Action, claim 15 is rejected as being unpatentable under 35 U.S.C. 103(a) in view of Szalay (2004), Molnar-Kimber (1999) and Harrison (2001), as applied to claims 2, 11-12 and 24-25 above, and further in view of Terman (2002).

The Examiner states that none of Szalay, Molnar-Kimber and Harrison teaches administration of carrier cells by intratumoral injection, but that Terman teaches the missing element. The Examiner concludes that it would have been obvious to the skilled artisan to combine the teachings of the noted publications to arrive at the present invention as claimed.

In response, reference is made to the comments above regarding the inability of Szalay to serve as legally-effective prior art.

None of Molnar-Kimber, Harrison and Terman, alone or in combination, teaches each element of claim 25, nor the additional element of intratumor injection recited in claim 15.

The Examiner has therefore not established a *prima facie* showing of obviousness under 35 U.S.C. §103(a) and Applicants respectfully request reconsideration and withdrawal of this rejection.

**C.** At page 14 of the Office Action, claims 6 and 16 are rejected as being unpatentable under 35 U.S.C. 103(a) in view of Szalay (2004), Molnar-Kimber (1999), Harrison (2001) and Terman (2002), as applied to claims 2, 11-12, 15 and 24-25 above, and further in view of Ochiya (2001).

The Examiner states that none of Szalay, Molnar-Kimber, Harrison and Terman teaches administration of atellocollagen with the oncolytic virus infected cells, but that Ochiya teaches the missing element. The Examiner concludes that it would have been obvious to the skilled artisan to combine the teachings of the noted publications to arrive at the present invention as claimed.

In response, reference is made to the comments above regarding the inability of Szalay to serve as legally-effective prior art.

None of Molnar-Kimber, Harrison, Terman and Ochiya, alone or in combination, teaches each element of claims 24 and 25, nor the additional element of atellocollagen recited in claims 6 and 16.

The Examiner has therefore not established a *prima facie* showing of obviousness under 35 U.S.C. §103(a) and Applicants respectfully request reconsideration and withdrawal of this rejection.

**D.** At page 15 of the Office Action, claim 5 is rejected as being unpatentable under 35 U.S.C. 103(a) in view of Szalay (2004), Molnar-Kimber (1999), Harrison (2001), Terman (2002) and Ochiya (2001), as applied to claims 2, 6, 11-12, 15, 16 and 24-25 above, and further in view of Hamada (2003).

The Examiner states that none of Szalay, Molnar-Kimber, Harrison, Terman and Ochiya teaches an oncolytic virus comprising a 1A1.3B promoter, but that Hamada

teaches the missing element. The Examiner concludes that it would have been obvious to the skilled artisan to combine the teachings of the noted publications to arrive at the present invention as claimed.

In response, reference is made to the comments above regarding the inability of Szalay to serve as legally-effective prior art.

None of Molnar-Kimber, Harrison, Terman, Ochiya and Hamada, alone or in combination, teaches each element of claims 24 and 25, nor the additional element of the 1A1.3B promoter recited in claim 5.

The Examiner has therefore not established a *prima facie* showing of obviousness under 35 U.S.C. §103(a) and Applicants respectfully request reconsideration and withdrawal of this rejection.

## VI. Conclusion

In view of the above amendments and remarks, Applicants respectfully request a Notice of Allowance. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at the below-listed telephone number.

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Respectfully submitted,

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Patent & Trademark Office

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